

REMARKS

Status of the Claims

Claims 4, 6, 7, 9-43, 49-59, 61, and 62 are pending. Claims 4, 6, 13, and 56 are amended above. The amendment also cancels claims 8 and 60. Claims 22-43, and 49-54 remain withdrawn.

Claim Objections

Claims 56 and 60 are objected to for allegedly failing to further limit the subject matter of a previous claim. This objection is moot in view of the above amendment, where claim 56 was amended to depend from claim 6, and 60 is canceled.

Thus Applicants respectfully submit that this objection should be withdrawn.

Issues Under 35 U.S.C. § 112, second paragraph

Claims 4, 6, and 13 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for “lacking essential steps.” This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested. The office action states that “[i]t is not clear to the Examiner as to how those skilled in the art “measure activity of COX-2 enzyme in a living subject.” This reasoning is not understood in view of the “relating step” featured in each of the rejected claims. Nevertheless, in view of the above amendment, the claims are presently at least “reasonably clear,” which is all that is required.

A claim is definite within the meaning of 35 U.S.C. § 112, second paragraph, if it sets out and circumscribes a particular subject matter with a reasonable degree of clarity and particularly.

See M.P.E.P. § 2173.02. Further, the USPTO is specifically instructed to “allow claims which define the patentable subject matter with a reasonable degree of particularly and distinctness. *Id.*

Claim 4 is rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for “lacking essential steps.” This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested. The office action states that “[i]t is not clear to the Examiner as to how those skilled in the art ‘relate’ the amount of PGH<sub>2</sub>-EA metabolite to the activity of COX-2 enzyme in the subject.”

The Federal Circuit, in a long line of cases, has made it clear that the definiteness of claim language must be analyzed not in a vacuum, but in light of the content of the particular application disclosure. For example, see *S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1369 (Fed. Cir. 2001), where the Court stated:

The purpose of the claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not “indefinite” simply because it is hard to understand when viewed with the benefit of the specification.

In the present office action, there appears to be no consideration of the specification, which is required, in making the assertion that one of ordinary skill in the art would not be able to make the “relation” discussed in the claim. Applicants respectfully submit that the claim language clearly satisfies the requirements of §112, second paragraph when they are examined as a whole in view of the specification as one of ordinary skill in the pertinent art.

However, in view of the above amendment to claim 4, this issue should be moot.

Claim 6 is rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for “lacking essential steps.” This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested. The office action states that “[i]t is not clear to the examiner as to how those skilled in the art can conclude that COX-2 activity in the subject is measured by detecting PGH<sub>2</sub>-EA metabolite in the subject.”

Again, there is no analysis in the office action that the claims were read and analyzed as a whole in view of the specification, which is required. Nonetheless, this rejection is moot in view of the amendment to claim 6, which includes a “comparing” step.

Claims 6 and 13 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for “lacking essential steps.” This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested. The office action states that “[i]t is not clear to the Examiner as to how those skilled in the art ‘relates the amount of COX-2 activity to a disease state or the progression of a disease state.’ ”

The same issues arise here as in the previous § 112, second paragraph rejections discussed above. Additionally, the issues raised are clearly moot in view of the above claim amendment, which includes the step of either comparing and relating a detected amount, or “associating the activity of the COX-2 enzyme to a disease state.” Applicants respectfully submit that these claim are reasonably precise when properly analyzed for compliance with 35 U.S.C. § 112, second paragraph.

Issues Under 35 U.S.C. § 102

Claim 4 is rejected under 35 U.S.C. § 102 as being allegedly anticipated by Yu et al.

This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

This reference is well discussed in the record. Yu et al. describe the enzymatic conversion of arachidonyl ethanolamine (anandamide, AEA) to PGE<sub>2</sub>-ethanolamide in cell lines expressing COX-2, but not COX-1.<sup>1</sup>

The deficiencies of Yu et al. vis-à-vis the present invention are many, and are discussed in the record and discussed in greater detail below. Additionally, with respect to the instant anticipation rejection, Applicants note that the office action states that Yu et al. disclose a method of “detecting/measuring COX-2 in a sample derived from a mammalian cell, which is a ‘living subject.’ ” Notwithstanding the problems and confusion inherent with the association that “a sample derived from a mammalian cell” is a “living subject” with an activity of a COX-2 enzyme, the present claims indicate that the activity of a COX-2 enzyme is measured in a mammalian subject. Applicants respectfully submit that this feature is clearly outside the scope of the cited reference.

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<sup>1</sup> See the specification at page 4. Also, see the Yu et al. abstract:

Incubation of anandamide with lysates and the intact cell line expressing COX-2 but not that of COX-1 produced prostaglandin E<sub>2</sub> ethanolamide. These results demonstrate the existence of a COX-2 mediated pathway for anandamide metabolism, and the metabolites formed represent a novel class of prostaglandins.

See Yu et al., at page 21181-2, especially the description entitled “Cell Culture,” which describes how the cultures of HFF cells were obtained, grown, and the treated to induce COX-2. There is no disclosure or even a suggestion of the claimed subjects.

Since the standard for anticipating a claim is that each and every element as set forth in the claim must be described in a single prior art reference, and be shown in as complete detail as is contained in the claim, this rejection should be withdrawn. See *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987) and *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989).

#### Issues Under 35 U.S.C. § 103

Claims 6-21, and 55-60 are rejected under 35 U.S.C. § 103 as allegedly being obvious over Yu et al., in view of Taketo et al. This rejection is respectfully traverse. Reconsideration and withdrawal thereof are requested.

The office action alleges that Yu et al. disclose “detecting/measuring COX-2 in a sample by detecting/measuring a PEGH<sub>2</sub>-EA metabolite [sic]...[and] generating a standard value and curve for detecting COX-2 activity.”

Applicants take strong issue with the Examiner’s reliance on Yu et al. in this manner. The office action reads way too much into the Yu et al. disclosure.

Initially, this rejection should be withdrawn because of the reliance on the improper “mammalian cell/living cell” interpretation as discussed above. Yu et al. grow cultured cells, then induce COX-2, then determine if the cultured cells metabolize COX-2. Applicants submit

that one way of looking at the Yu et al. method is starting with COX-2 activity, and then see if it metabolizes AA and AEA.

Additionally, the office action improperly states that the Yu et al. disclosure “generates a standard value or curve.” Figure 1 of Yu et al., relied on in the office action for this assertion, shows AA and AEA oxygen consumption. The discussion of this figure in the reference states that the data show, *inter alia*, binding site competition between AA and AEA.

Applicants respectfully submit that no proper *prima facie* case can be established with a detailed showing of how the information of Figure 1 is equated with the claimed “comparing” and “associating” steps.

Additionally, the motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. Applicants submit that in the present case, no proper *prima facie* can be made without impermissible hindsight by not addressing the fact that Yu et al. fail to disclose or suggest the downstream metabolites of the present invention and the significance of their presence and quantification. The relevance of the fact that Yu et al state that “At the present time the physiological significance of the metabolism of AEA by COX-2 is not known.” See page 21186.

The many deficiencies of Yu et al. are not remedied by the secondary reference, which is apparently relied on for the notion that “COX-2 expression is increased in cancerous cells.”

From the foregoing, further and favorable reconsideration in the form of a Notice of Allowability is believed to be in order, and such action is earnestly solicited.

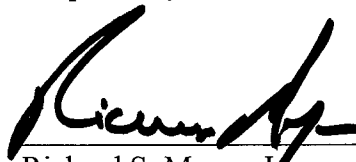
Interview Requested

It is clear from the record that a personal interview will expedite the prosecution of this application – particularly with respect to eliminating the applicability of the Yu et al. reference.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for a three-month extension of time for filing a response to the outstanding Office Action. Payment of the extension fee in the amount of \$510.00 was authorized with the electronic filing of this amendment.

If the Examiner has any questions concerning this amendment or the application in general, he is requested to contact the undersigned at the number listed below.

Respectfully submitted,



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